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Impact of Percutaneous Nephrolithotomy on Estimated Glomerular Filtration Rate in Patients with Chronic Kidney Disease

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ABSTRACT

***Background and Purpose*: We investigated the impact of percutaneous renal procedures on estimated glomerular filtration rate (GFR) of patients with chronic kidney disease (CKD).**

***Patients and Methods*: The GFRs of adult patients were calculated using the Modification of Diet in Renal Disease formula, and the patients were staged according to the Kidney Disease Outcome Quality Initiative CKD classification system. The study included 185 patients with preoperative GFR values less than 60 mL/min/1.73 m^2. The impact of percutaneous nephrolithotomy (PCNL) on GFR was analyzed by comparing the preoperative GFR with the GFR before discharge and at postoperative month 3.**

***Results*: Patients with CKD had a significant increase in the GFR after the procedure. In postoperative month 3, the mean GFR was more than 60 mL/min/1.73 m^2 in 25% of the patients with CKD and less than 60 mL/min/1.73 m^2 in 75%. While all patients with stage 5 CKD improved to better stages, some other patients' conditions declined to stage 5 from better stages at the end of postoperative month 3. No patient needed dialysis. The presence of urinary tract infections tended to affect GFR negatively.**

***Conclusion*: Estimated GFR, as a better indicator of renal function, is significantly affected by the PCNL procedure. While significant improvement was observed in late-stage patients with CKD, unexpected deterioration could occur in patients at earlier stages.**

INTRODUCTION

URINARY STONE DISEASE has a prevalence of 1.7% to 18% in patients with chronic kidney disease (CKD),[1,2] and nephrolithiasis-related CKD contributed to 3.2% of the total patients who started maintenance dialysis therapy.[3] Management of urinary stone disease in patients with CKD is often very difficult. Options for preserving kidney function include watchful waiting, shockwave lithotripsy (SWL), an endourologic approach, and laparoscopic or conventional open surgery.

Watchful waiting usually leads to the progressive loss of functioning renal tissue. SWL has limitations in poorly functioning kidneys.[4] Any surgical intervention is complicated in the presence of azotemia and may result in injury to renal parenchyma. Percutaneous endourologic procedures are the most suitable option and cause minimum morbidity and mortality.[5]

While the serum creatinine level has often been used as a crude index of renal function in studies of patients with CKD, it is not reliable. The glomerular filtration rate (GFR) should be used instead. GFR is the most accurate way to give health providers an estimate of functioning renal mass. Estimating GFR with the use of prediction equations is cost effective. The Modification of Diet in Renal Disease (MDRD) formula for the estimation of GFR is recommended for routine use by the Kidney Disease Outcome Quality Initiative (K/DOQI) of the National Kidney Foundation.[6]

We present our experience with percutaneous nephrolithotomy (PCNL) in patients with CKD who have upper urinary tract calculi and were classified according to the K/DOQI CKD classification system (Table 1).

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Table 1. Stages of Chronic Kidney Disease According to the K/DOQI CKD (Chronic Kidney Disease) Classification System

Stage	*Description*	*GFR (mL/min/1.73 m²)*
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

GFR = glomerular filtration rate.

PATIENTS and METHODS

Between October 1998 and May 2006, we performed 1821 PCNL procedures in 1745 patients at two centers. Among them, 185 patients (11.3%) had preoperative GFR values less than 60 mL/min/1.73 m^2 (Table 2). Preoperative assessment included history and physical examination, urine microscopy, urine culture and sensitivity, plain radiography (kidneys, ureters, bladder [KUB]), ultrasonography of the kidneys and bladder, and serum creatinine and electrolyte measurements. Studies including CT and renal scintigraphy were not routinely performed. CT was used to delineate the complex anatomy of the kidney or stones in selected patients. Calculus size was calculated with a computer running commercially available software and is reported in mm^2.

All patients with evidence of obstruction had placement of a nephrostomy tube (single or multiple) or Double-J stent before definitive surgical intervention. After stabilization of the serum creatinine level and after relief of the obstruction (documented by clinical remission, radiologic improvement, and decreased serum creatinine level), the GFR was calculated and PCNL for stone removal was performed. Patients with urinary-tract infections were treated with appropriate antibiotics for at least 1 week before surgery, and the therapy was completed in 3 weeks.

PCNL was performed with patients in the prone position under general anesthesia after insertion of a ureteral catheter to the affected site. Renal access was gained with fluoroscopic guidance, and tract dilatation was performed using Amplatz dilators. Pneumatic, ultrasonic, and laser lithotripters were used for *in situ* stone fragmentation, alone or in combination. All patients left the operating room with a re-entry catheter.

Each patient was evaluated routinely with plain KUB radiography and serum biochemistry before discharge. All patients were scheduled for the first follow-up visit at postoperative month 3 with stone analysis, serum biochemistry, urine culture, and radiologic studies according to the stone composition. Stone-free rates were assessed accordingly. CT of the abdomen was indicated only for kidneys with nonopaque and semiopaque stones. Further follow-up and treatment were individualized.

The files of the patients were retrospectively evaluated and preoperative/postoperative GFRs of the adult patients were calculated using the MDRD formula. Then, patients were staged according to the K/DOQI CKD classification system. Special factors that affect the difficulty of treatment, such as aberrant anatomy, a solitary kidney, polycystic disease, or a transplanted kidney, were noted. Characteristics of the calculi, clinical outcome, and follow-up serum creatinine level were also analyzed.

The effectiveness and complications of PCNL in patients with CKD were also documented. The impact of PCNL on estimated GFR was analyzed by comparing the estimated preoperative GFR with the GFR at discharge and at postoperative month 3. Stage migration of the patients and factors affecting GFR changes were analyzed in 130 patients who were monitored for at least 3 months. The effect on outcome of various factors, including gender, stone composition, volume, and localization, number of accesses, surgery time, presence of a solitary kidney, complications, and residual stones were examined. The Student *t* test , Mann Whitney-U test, chi-square test, and general linear model with repeated measures test were used for statistical analysis, and a *P* value of 0.05 was considered statistically significant.

RESULTS

Demographic and calculi data of the CKD patients are summarized in Table 2. In total, 196 procedures were performed in

Table 2. Demographic and Stone Data of the CKD Patients

Number of patients	185
Number of involved renal units	196
Mean age	53.2 (20–81)
Sex (M/F)	108/77
Calculus type	
Opaque	170 (86.7)
Semiopaque	11 (5.6)
Nonopaque	15 (7.7)
Mean calculus size	779.8 (16–4900) mm^2
Calculus localization	
Pelvis	33 (16.9)
Pelvis + other calix	48 (24.6)
Upper pole	4 (2.1)
Midpolar	8 (4.1)
Lower pole	37 (19.0)
Multicaliceal	18 (9.2)
Staghorn	45 (23.1)
Upper ureter	2 (1)
Previous stone treatment	
Primary	129 (66.2)
Secondary	48 (24.6)
Tertiary	18 (9.1)
Quaternary	1 (0.5)
Associated illness	
HT	16
DM	3
CAD	6
COPD	4
UTI	41
Preoperative diversion	9
Dialysis	None

HT = hypertension; DM = diabetes mellitus; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; UTI = urinary-tract infection.

Table 3. Perioperative and Postoperative Data of Patients with Chronic Kidney Disease

Surgery time (minutes)	101.4 (10–250)
Anesthesia time (minutes)	137 (40–300)
Fluoroscopy time (minutes)	4.5 (0.44–12)
Number of accesses	
1	134 (68.4%)
2	40 (20.4%)
3	13 (6.6%)
4	4 (2%)
5	2 (1%)
6	3 (1.5%)
Complications	
Hydro/hemothorax (%)	1
Fever (%)	15
Hg drop (mg/dL)	1.43 (0–7.6)
Blood transfusion (%)	36
Stone migration (%)	1
Colonic perforation (%)	1
Urinary drainage (%)	7
Sepsis (%)	3
Death (%)	2
Hospital stay (days)	5.8 (1–36)
Stone-free rate	159 (81.1%)

Hg = hemoglobin.

185 patients with CKD (108 men, 77 women). The mean preoperative serum creatinine level was 1.87 mg/dL (range 1–6.5 mg/dL). Among the CKD group, 39 patients had a solitary kidney, including two transplanted kidneys. Forty-five patients had a complete or partial staghorn calculus. Urinary-tract infection and hypertension were the leading comorbidities. Nearly 35% of patients had had previous stone treatment.

The operative data are summarized in Table 3. Of the 185 patients in the CKD group, 66 (35.6%) had one or more complications. More than one access was performed in 32% of patients. Three patients had sepsis and two died. One colonic perforation and one hemothorax were managed conservatively. While 36% of patients needed blood transfusion, one patient underwent selective embolization for bleeding. The prevalence of anemia (hemoglobin lower than 12 g/dL) in this group was 37.8%. The mean preoperative hemoglobin level was significantly lower in transfused patients (11.9 g/dL *v* 13.4 g/dL).

Complete stone-free status was achieved in 81.1%. Clinically significant residual stones (>5 mm) were present in 21 renal units (10.7%); insignificant residual fragments were present in the remaining 16 (8.1%). In all, 5 renal units underwent adjuvant SWL treatment, 10 had second-look PCNL, and 5 underwent ureteroscopy.

There was a significant increase in the GFR at discharge ($P < 0.000$) (Table 4). Renal function improved (GFR more than 60 mL/min/1.73 m^2) after 39 procedures (19.9%), and GFR remained less than 60 mL/min/1.73 m^2 after 157 procedures (79.5%) (Table 5). Analysis of all patients in each stage showed an increase in GFR from a mean value of 47.4 mL/min/1.73 m^2 to 53.8 mL/min/1.73 m^2 ($P = 0.02$), from 21.7 mL/min/1.73 m^2 to 28.9 mL/min/1.73 m^2 ($P = 0.01$), and from 11.2 mL/min/1.73 m^2 to 27.4 mL/min/1.73 m^2 ($P = 0.03$) in stage 3, 4, and 5 patients, respectively.

Reevaluation of patients at the first follow-up visit at postoperative month 3 was available for only 130 patients. GFR was more than 60 mL/min/1.73 m^2 in 25% of the patients with CKD and less than 60 mL/min/1.73 m^2 in 75%. While all four patients with stage 5 CKD improved to better stages, five other patients' conditions declined to stage 5 from better stages at the end of postoperative month 3 without evidence of obstruction (two from stage 4 and three from stage 3) (Table 5).

Excluding age and serum creatinine level, which were used for GFR calculation, none of the analyzed factors (sex, stone composition, volume, localization, number of accesses, surgery time, presence of a solitary kidney, complications, and residual stones) had an effect on outcome. Only the presence of urinary-tract infections had a tendency to negatively affect the GFR ($P = 0.07$).

Postoperative fever occurred in 15 patients with CKD, including 5 with documented nosocomial infection (*Pseudomonas aeruginosa* in 2, *Escherichia coli* in 1, methicillin-resistant *Staphylococcus aureus* in 1, and enterococci in 1). The rate of sepsis and sepsis-related mortality (two patients died) was high in the patients with CKD. Severe sepsis developed in three patients; two of these patients died.

DISCUSSION

CKD is a major public health problem. Early recognition of CKD and management of its underlying factors could help pre-

Table 4. Renal Function Parameters of Patients with CKD during 3-Month Follow-Up

	Preoperative[a]	*Before discharge*	*Postoperative month 3*	P
Creatinine	1.87 (1–4.6)	1.68 (0.2–5.7)	1.69 (0.78–5.30)	<0.05
GFR	42.4 (6.4–58.9)	49.3 (9.6–240)	48.4 (12.5–108.3)	<0.05
CKD stage				
1	—	3 (1.5)	3 (2.3)	
2	—	36 (18.4)	30 (23.1)	<0.05
3	161 (82.1)	128 (65.3)	76 (58.5)	
4	28 (14.3)	24 (12.2)	16 (12.3)	
5	7 (3.6)	5 (2.6)	5 (3.8)	
N	196	196	130	

[a]The group responsible for the statistical difference.
GFR = glomerular filtration rate; CKD = chronic kidney disease.

Table 5. Stage Migration after Percutaneous Management of Stones in Patients with CKD at Discharge and Month 3

	CKD stages at discharge					
	1	*2*	*3*	*4*	*5*	*Total*
Preoperative CKD stages						
3	3	34	118	6	0	161
4	0	2	6	17	3	28
5	0	0	4	1	2	7
Total	3	36	128	24	5	196
	Postoperative month 3 CKD stages					
	1	*2*	*3*	*4*	*5*	*Total*
Preoperative CKD stages						
3	2	27	64	14	3	110
4	1	3	8	2	2	16
5	0	0	4	0	0	4
Total	3	30	76	16	5	130

CKD = chronic kidney disease.

vent such adverse outcomes as the expense of long-term hemodialysis and transplantation, as well as social and psychological trauma. CKD is an uncommon event among stone formers, but nephrolithiasis-related CKD accounts for a significant percentage of patients for whom renal replacement therapy is necessary.[7] It has been assumed that CKD will develop in 3 of 100,000 stone formers annually.[3]

In a cohort of 171 patients with severe idiopathic calcium stone disease, Marangella and associates[8] reported that 18% had mild renal insufficiency, with a mean GFR of 67 mL/min/1.73 m^2 at referral, but there was not a significant decline during a mean follow-up of nearly 3.5 years.[8] Similarly, of 3266 patients with nephrolithiasis reported by Worcester and colleagues,[9] CKD did not develop in any patient, and there was not a significant decline in creatinine clearances between the first and last follow-up visits. On the other hand, Worcester and coworkers[9] reported that renal function determined by creatinine clearance decreases with age in stone formers at a higher rate than in non-stone-formers, and that patients with kidney stones do not have normal kidney function compared with healthy individuals. Therefore, in clinical management, all efforts must be made to minimize renal injury while balancing the risks of obstruction from stones against those of urologic procedures.

Accurate estimation of GFR is crucial for the detection of CKD. Creatinine is still widely measured for the prediction of GFR, despite its inaccuracy. Creatinine levels are affected by many factors other than glomerular function, including overall muscle bulk, medications, tubular creatinine secretion, and nonrenal creatinine secretion.[10] Serum creatinine concentrations can be within the normal range even with a GFR around 60 mL/min/1.73 m^2, which results in a "creatinine-blind range."[10] As a result, the serum creatinine level tends to overestimate kidney function. In a study by Papadakis and associates,[11] the serum creatinine level was within the normal range in each of 15 patients with cirrhosis, despite a marked reduction in GFR.

In guidelines for the diagnosis and classification of CKD, the K/DOQI of the National Kidney Foundation recommends use of the MDRD equation for predicting renal function and for the diagnosis of CKD.[6] The MDRD equation estimates the level of GFR by taking into account the serum creatinine concentration and some or all of the following variables: age, sex, race, and body size.[12] This equation does not need a timed urine collection and is more accurate than both blood creatinine and measured creatinine clearance.[6]

Thus, studies of patients with CKD should not be evaluated solely on the serum creatinine level, and the stage of disease should be assigned based on the level of kidney function, irrespective of diagnosis, according to the K/DOQI CKD classification system. Our study population was composed of patients with stone disease in whom PCNL treatment was indicated; 11.2% had mild to severe renal failure according to the MDRD formula. If renal insufficiency was defined as a baseline serum creatinine level less than 1.5 mg/dL, we would have missed 79 (42.7%) patients with different degrees of CKD.

Most agree that stones in patients with CKD should be cleared.[13–16] Paryani and coworkers[15] reported that, especially in patients with mild to moderate renal insufficiency, an aggressive approach was needed to render them stone free, which would improve renal function. SWL has a limited role in patients with CKD who have stone disease.[4,5] PCNL is the primary modality for treating patients with CKD; however, it is not without complications.[5] Hypothermia, bleeding, metabolic acidosis, disturbances in serum electrolytes, urosepsis, and even death are the main complications.

Despite prophylactic antibiotics, urosepsis remains a major concern, even in patients with CKD who have sterile preoperative urine cultures.[5] Because of the inhibition of cell-mediated immunity and humoral defense mechanisms, septicemia can easily develop in patients with CKD. Agrawal and associates[14] reported a mortality rate caused by sepsis of 3.8% among 78 patients with advanced uremia who were treated for urolithia-

sis by PCNL. In the present study, despite receiving appropriate antibiotics, septic shock developed in three patients; only one was saved with intensive treatment. Our mortality rate was 1.1%, and all deaths were caused by sepsis.

Our overall complication rate was also high in patients with CKD. Bleeding was the leading problem. The need for multiple access tracts reflects rather complicated stones. Complicated stones are associated with poorer results; necessitate longer operative time, multiple percutaneous tracts, and more ancillary procedures; and have a higher complication rate. Furthermore, underlying platelet dysfunction could also have a role in clinically significant bleeding. Anemia in these patients has also played a role in the high rate of transfusion.

There have been some attempts to identify predictors of prognosis and treatment outcome in patients with CKD who have upper urinary-tract calculi. Kukreja and colleagues[13] reported that the significant factors in predicting deterioration of renal function were a higher baseline preoperative serum creatinine level, proteinuria more than 300 mg/d on follow-up, renal cortical atrophy, stone burden greater than 1500 mm^2, recurrent urinary infection, and time elapsed after PCNL surgery of less than 15 years.

In another study, Agrawal and coworkers[14] described the predictors of recovery as parenchymal thickness of 7 mm, clear urine in the collecting system, no renal sepsis, and recent onset azotemia. In the present study, complete stone clearance was achieved in 81.1% of the renal units, and the mean preoperative GFR significantly increased from 42.4 mL/min/1.73 m^2 to 48.4 mL/min/1.73 m^2 in postoperative month 3. None of the patients in our series needed dialysis. Although the previously mentioned factors were not documented in our study, of the available studied factors, only the presence of urinary-tract infections had a tendency to have a negative effect on GFR.

To account for stage-related differences in the present study, we analyzed the course of renal function separately, according to the K/DOQI CKD classification system. We found that nearly all of the patients at the last stage of CKD had a net benefit from surgery; however, while 50% of stage 4 patients improved, only 25% of stage 3 patients showed improvement. Renal function gain was the greatest in stage 5 patients, the least in stage 2, and moderate in stage 4 patients.

One could speculate that the impact of a stone in a severely compromised kidney is greater than the impact of PCNL, while the reverse is true for moderately affected kidneys in which the impact of PCNL may be more deleterious. This deleterious effect may be augmented by persistent urinary-tract infection. Although stage migrations were observed at the 3-month follow-up, the net benefit on GFR on postoperative day 3 remained stable and unchanged at postoperative month 3.

CONCLUSION

Nephrolithiasis remains the cause of potentially avoidable CKD in many patients, despite major advances in diagnosis and management. The serum creatinine level alone does not accurately indicate reserved renal function. Estimated GFR, as a better indicator of renal function, is significantly affected by the PCNL procedure. While significant improvement was observed in late-stage CKD patients, unexpected deterioration could occur in patients at earlier stages. Although it is not statistically proven, strict control of urinary-tract infection in this group of patients may be as beneficial as PCNL.

The overall benefit of PCNL was evident, although the complication rate and mortality risk were high in these patients. Therefore, one may expect that aggressive treatment of such patients could prevent the need for renal replacement therapy, or at least significantly delay it in most patients with renal stone disease.

REFERENCES

1. Marangella M, Tricerri A, Bruno M, Vitale C, Bianco O, Martini C, Linari F. [Nephrolithiasis due to infections. Analysis of the mode and factors of progression toward renal failure.] (Ita) Minerva Urol Nefrol 1986;38:103–106.
2. Gupta M, Bolton DM, Gupta PN, Stoller ML. Improved renal function following aggressive treatment of urolithiasis and concurrent mild to moderate renal insufficiency. J Urol 1994;152:1086–1090.
3. Jungers P, Joly D, Barbey F, Choukroun G, Daudon M. ESRD caused by nephrolithiasis: Prevalence, mechanisms, and prevention. Am J Kidney Dis 2004;44:799–805.
4. Lingeman J E, Woods J, Toth PD, Evan AP, McAteer JA. The role of lithotripsy and its side effects. J Urol 1989;141:793.
5. Gopalakrishnan G, Prasad GS. Management of urolithiasis with chronic renal failure. Curr Opin Urol 2007;17:132–135.
6. Eknoyan G, Levin NW. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Foreword. Am J Kidney Dis 2002;39:S14.
7. Gambaro G, Favaro S, D'Angelo A. Risk for renal failure in nephrolithiasis. Am J Kidney Dis 2001;37:233–243.
8. Marangella M, Bruno M, Cosseddu D, Manganaro M, Tricerri A, Vitale C, Linari F. Prevalence of chronic renal insufficiency in the course of idiopathic recurrent calcium stone disease: Risk factors and patterns of progression. Nephron 1990;54:302–306.
9. Worcester E, Parks JH, Josephson MA, Thisted RA, Coe FL Causes and consequences of kidney loss in patients with nephrolithiasis. Kidney Int 2003;64:2204–2213.
10. Perrone RD, Madias NE, Levey AS. Serum creatinine as an index of renal-function: New insights into old concepts. Clin Chem 1992; 38:1933–1953.
11. Papadakis MA, Arieff AI. Unpredictability of clinical evaluation of renal function in cirrhosis. Prospective-study. Am J Med 1987; 82:945–952.
12. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: A new prediction equation. Ann Intern Med 1999; 130:461–470.
13. Kukreja R, Desai M, Patel SH, Desai MR. Nephrolithiasis associated with renal insufficiency: Factors predicting outcome. J Endourol 2003;17:875–879.
14. Agrawal MS, Aron M, Asopa HS. Endourological renal salvage in patients with calculus nephropathy and advanced uraemia. BJU Int 1999;84:252–256.
15. Paryani JP, Ather MH. Improvement in serum creatinine following definite treatment of urolithiasis in patients with concurrent renal insufficiency. Scand J Urol Nephrol 2002;36:134–136.
16. Singh I, Gupta NP, Hemal AK, Aron M, Dogra PN, Seth A. Efficacy and outcome of surgical intervention in patients with nephrolithiasis and chronic renal failure. Int Urol Nephrol 2001;33:293–298.

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ABBREVIATIONS USED

CKD = chronic kidney disease
CT = computed tomography
GFR = glomerular filtration rate
K/DOQI = Kidney Disease Outcome Quality Initiative
KUB = kidneys, ureters, bladder
MDRD = Modification of Diet in Renal Disease
PCNL = percutaneous nephrolithotomy
SWL = shockwave lithotripsy

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1. Akbar Nouralizadeh, Mehrdad Mohammadi Sichani, Amir H. Kashi. 2011. Impacts of percutaneous nephrolithotomy on the estimated glomerular filtration rate during the first few days after surgery. *Urological Research* **39**:2, 129-133. [CrossRef]
2. Shun-Fa Hung, Shiu-Dong Chung, Shuo-Meng Wang, Hong-Jeng Yu, Ho-Shiang Huang. 2010. Chronic kidney disease affects the stone-free rate after extracorporeal shock wave lithotripsy for proximal ureteric stones. *BJU International* **105**:8, 1162-1167. [CrossRef]